

# SEQUENCE LISTING

<110> POLONSKY, KENNETH S.  
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 ODA, NAOHISA  
 COX, NANCY J.  
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 OTANI, KENICHI  
 HANIS, CRAIG L.  
 BELL, GRAEME I.

<120> METHODS OF TREATMENT OF TYPE 2 DIABETES

<130> ARCD:307

<140> UNKNOWN

<141> 1999-10-21

<150> 60/134,175

<151> 1999-05-13

60/105,052

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<160> 30

<170> PatentIn Ver. 2.0

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 Ser Arg Leu His Ala Ala Asp Trp Ala Gly Arg Ala Arg Ala Leu Val  
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 Gly Asp Ser His Thr Ser Trp Ser Pro Ala Ser Ile Pro Gly Lys His  
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Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
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Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg
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Ile Trp Gln Phe Gly Arg Trp Val Glu Val Thr Thr Asp Asp Arg Leu
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Val Phe Trp Leu Pro Leu Leu Glu Lys Val Tyr Ala Lys Val His Gly
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Leu Thr Gly Gly Leu Ala Glu Arg Trp Asn Leu Lys Gly Val Ala Gly
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Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln  
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Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala  
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Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly  
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Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg  
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Ile Trp Gln Phe Gly Arg Trp Val Glu Val Thr Thr Asp Asp Arg Leu  
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Ser Gly Gly Gln Gln Asp Arg Pro Gly Arg Trp Glu His Arg Thr Cys  
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<211> 513

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<213> Human

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Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
      50             55            60

Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
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Val	Thr	Glu	Ala	Gly	His	Leu	Gln	Ser	Leu	Tyr	Thr	Glu	Arg	Leu	Leu	
				325					330					335		
Cys	His	Thr	Arg	Ala	Leu	Pro	Gly	Ala	Trp	Val	Lys	Gly	Gln	Ser	Ala	
			340					345					350			
Gly	Gly	Cys	Arg	Asn	Asn	Ser	Gly	Phe	Pro	Ser	Asn	Pro	Lys	Phe	Trp	
		355					360					365				
Leu	Arg	Val	Ser	Glu	Pro	Ser	Glu	Val	Tyr	Ile	Ala	Val	Leu	Gln	Arg	
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Ser Arg Leu His Ala Ala Asp Trp Ala Gly Arg Ala Arg Ala Leu Val  
385 390 395 400

Gly Asp Ser His Thr Ser Trp Ser Pro Ala Ser Ile Pro Gly Lys His  
405 410 415

Tyr Gln Ala Val Gly Leu His Leu Trp Lys Val Glu Lys Arg Arg Val  
420 425 430

Asn Leu Pro Arg Val Leu Ser Met Pro Pro Val Ala Gly Thr Ala Cys  
435 440 445

His Ala Tyr Asp Arg Glu Val His Leu Arg Cys Glu Leu Ser Pro Gly  
450 455 460

Tyr Tyr Leu Ala Val Pro Ser Thr Phe Leu Lys Asp Ala Pro Gly Glu  
465 470 475 480

Phe Leu Leu Arg Val Phe Ser Thr Gly Arg Val Ser Leu Arg Ser Gln  
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Cys

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<211> 2204  
<212> DNA  
<213> Human

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 <211> 444  
 <212> PRT  
 <213> Human

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Ala Ala Phe Pro Ala Ala Asp Ser Ser Leu Phe Cys Asp Leu Ser Thr
      20             25             30

Pro Leu Ala Gln Phe Arg Glu Asp Ile Thr Trp Arg Arg Pro Gln Glu
      35             40             45

Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
      50             55             60

Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
      65             70             75             80

Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly
      85             90             95

Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg
      100            105            110

Ile Trp Gln Phe Gly Arg Trp Val Glu Val Thr Thr Asp Asp Arg Leu
      115            120            125

Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp
      130            135            140

Val Phe Trp Leu Pro Leu Leu Glu Lys Val Tyr Ala Lys Val His Gly
      145            150            155            160

Ser Tyr Glu His Leu Trp Ala Gly Gln Val Ala Asp Ala Leu Val Asp
      165            170            175

Leu Thr Gly Gly Leu Ala Glu Arg Trp Asn Leu Lys Gly Val Ala Gly
      180            185            190

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Ser Gly Gly Gln Gln Asp Arg Pro Gly Arg Trp Glu His Arg Thr Cys  
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 Arg Gln Leu Leu His Leu Lys Asp Gln Cys Leu Ile Ser Cys Cys Val  
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 Leu Ser Pro Arg Ala Gly Ala Arg Glu Leu Gly Glu Phe His Ala Phe  
 225 230 235 240  
 Ile Val Ser Asp Leu Arg Glu Leu Gln Gly Gln Ala Gly Gln Cys Ile  
 245 250 255  
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 260 265 270  
 Leu Trp Arg Glu Gly Gly Glu Gly Trp Ser Gln Val Asp Ala Ala Val  
 275 280 285  
 Ala Ser Glu Leu Leu Ser Gln Leu Gln Glu Gly Glu Phe Trp Val Glu  
 290 295 300  
 Glu Glu Glu Phe Leu Arg Glu Phe Asp Glu Leu Thr Val Gly Tyr Pro  
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 Val Thr Glu Ala Gly His Leu Gln Ser Leu Tyr Thr Glu Arg Leu Leu  
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 Cys His Thr Arg Ala Leu Pro Gly Ala Trp Val Lys Gly Gln Ser Ala  
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 Gly Gly Cys Arg Asn Asn Ser Gly Phe Pro Ser Asn Pro Lys Phe Trp  
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 370 375 380  
 Ser Arg Leu His Ala Ala Asp Trp Ala Gly Arg Ala Arg Ala Leu Val  
 385 390 395 400  
 Gly Asp Ser His Thr Ser Trp Ser Pro Ala Ser Ile Pro Gly Lys His  
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 <211> 2516  
 <212> DNA  
 <213> Human

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 <211> 274  
 <212> PRT  
 <213> Human

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 20 25 30  
 Pro Leu Ala Gln Phe Arg Glu Asp Ile Thr Trp Arg Arg Pro Gln Glu  
 35 40 45  
 Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln

50	55	60
Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala 65 70 75 80		
Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly 85 90 95		
Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg 100 105 110		
Ile Trp Gln Phe Gly Arg Trp Val Glu Val Thr Thr Asp Asp Arg Leu 115 120 125		
Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp 130 135 140		
Val Phe Trp Leu Pro Leu Leu Glu Lys Gly Pro Trp Val Leu Arg Ala 145 150 155 160		
Pro Val Gly Arg Ala Gly Gly Gly Cys Pro Gly Gly Pro Asp Arg Arg 165 170 175		
Pro Gly Arg Lys Met Glu Pro Glu Gly Arg Ser Arg Lys Arg Arg Pro 180 185 190		
Ala Gly Gln Ala Arg Pro Leu Gly Ala Gln Asp Leu Ser Ala Ala Ala 195 200 205		
Pro Pro Glu Gly Pro Val Ser Asp Gln Leu Leu Arg Ala Gln Pro Gln 210 215 220		
Ser Arg Cys Pro Gly Ala Gly Gly Val Pro Cys Leu His Cys Leu Gly 225 230 235 240		
Pro Ala Gly Ala Pro Gly Ser Gly Gly Pro Val His Pro Ala Ala Ala 245 250 255		
Asp Pro Glu Pro Leu Gly Pro Ala Val Leu Ala Gly Ala Leu Glu Arg 260 265 270		

Gly Gly

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 <211> 2455  
 <212> DNA  
 <213> Human

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 <211> 139  
 <212> PRT  
 <213> Human

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<400> 14
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Ala Ala Phe Pro Ala Ala Asp Ser Ser Leu Phe Cys Asp Leu Ser Thr
      20             25             30

Pro Leu Ala Gln Phe Arg Glu Asp Ile Thr Trp Arg Arg Pro Gln Glu
      35             40             45

Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
      50             55             60

Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
      65             70             75             80

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Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ser Cys Pro Val  
85 90 95

Gln Leu Pro Ala Asp Trp Thr Cys Lys Val Gln Pro Val Trp Leu Glu  
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Phe Pro Cys Leu Pro Ile Ser Cys Arg Leu Arg Val Ser Ser Asp Thr  
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Ser Pro Asp Ser Ala Thr Trp Gly Ser Trp Lys  
130 135

<210> 15  
<211> 1267  
<212> DNA  
<213> Human

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<211> 138  
<212> PRT  
<213> Human

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Pro Leu Ala Gln Phe Arg Glu Asp Ile Thr Trp Arg Arg Pro Gln Val  
35 40 45



Pro Glu Gly Gly Arg Ser Gln Asp Ala Pro Pro Leu Leu Leu Gln Glu  
50 55 60

Pro Leu Leu Ser Cys Val Pro His Arg Tyr Ala Gln Glu Val Ser Arg  
65 70 75 80

Leu Cys Leu Leu Pro Ala Gly Thr Tyr Lys Val Val Pro Ser Thr Tyr  
85 90 95

Leu Pro Asp Thr Glu Gly Ala Phe Thr Val Thr Ile Ala Thr Arg Ile  
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Asp Arg Pro Ser Ile His Ser Gln Glu Met Leu Gly Gln Phe Leu Gln  
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Glu Val Ser Val Met Ala Val Met Lys Thr  
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<211> 864  
<212> DNA  
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Thr Leu Leu His Arg Val Val Pro His Gly Gln Ser Phe Gln Asn Gly		
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Tyr Ala Gly Ile Phe His Phe Gln Leu Trp Gln Phe Gly Glu Trp Val		
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Asp Val Val Val Asp Asp Leu Leu Pro Ile Lys Asp Gly Lys Leu Val		
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Phe Val His Ser Ala Glu Gly Asn Glu Phe Trp Ser Ala Leu Leu Glu		
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Lys Ala Tyr Ala Lys Val Asn Gly Ser Tyr Glu Ala Leu Ser Gly Gly		
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Arg	Arg	Gln	Arg	Lys	Met	Gly	Glu	Asp	Met	His	Thr	Ile	Gly	Phe	Gly	420	425	430
Ile	Tyr	Glu	Val	Pro	Glu	Glu	Leu	Ser	Gly	Gln	Thr	Asn	Ile	His	Leu	435	440	445
Ser	Lys	Asn	Phe	Phe	Leu	Thr	Asn	Arg	Ala	Arg	Glu	Arg	Ser	Asp	Thr	450	455	460
Phe	Ile	Asn	Leu	Arg	Glu	Val	Leu	Asn	Arg	Phe	Lys	Leu	Pro	Pro	Gly	465	470	475
Glu	Tyr	Ile	Leu	Val	Pro	Ser	Thr	Phe	Glu	Pro	Asn	Lys	Asp	Gly	Asp	485	490	495

Phe Cys Ile Arg Val Phe Ser Glu Lys Lys Ala Asp Tyr Gln Ala Val  
 500 505 510  
 Asp Asp Glu Ile Glu Ala Asn Leu Glu Glu Phe Asp Ile Ser Glu Asp  
 515 520 525  
 Asp Ile Asp Asp Gly Val Arg Arg Leu Phe Ala Gln Leu Ala Gly Glu  
 530 535 540  
 Asp Ala Glu Ile Ser Ala Phe Glu Leu Gln Thr Ile Leu Arg Arg Val  
 545 550 555 560  
 Leu Ala Lys Arg Gln Asp Ile Lys Ser Asp Gly Phe Ser Ile Glu Thr  
 565 570 575  
 Cys Lys Ile Met Val Asp Met Leu Asp Ser Asp Gly Ser Gly Lys Leu  
 580 585 590  
 Gly Leu Lys Glu Phe Tyr Ile Leu Trp Thr Lys Ile Gln Lys Tyr Gln  
 595 600 605  
 Lys Ile Tyr Arg Glu Ile Asp Val Asp Arg Ser Gly Thr Met Asn Ser  
 610 615 620  
 Tyr Glu Met Arg Lys Ala Leu Glu Glu Ala Gly Phe Lys Met Pro Cys  
 625 630 635 640  
 Gln Leu His Gln Val Ile Val Ala Arg Phe Ala Asp Asp Gln Leu Ile  
 645 650 655  
 Ile Asp Phe Asp Asn Phe Val Arg Cys Leu Val Arg Leu Glu Thr Leu  
 660 665 670  
 Phe Lys Ile Phe Lys Gln Leu Asp Pro Glu Asn Thr Gly Thr Ile Glu  
 675 680 685  
 Leu Asp Leu Ile Ser Trp Leu Cys Phe Ser Val Leu  
 690 695 700

<210> 24  
 <211> 821  
 <212> PRT  
 <213> Human

<400> 24

Met Pro Thr Val Ile Ser Ala Ser Val Ala Pro Arg Thr Ala Ala Glu  
 1 5 10 15  
 Pro Arg Ser Pro Gly Pro Val Pro His Pro Ala Gln Ser Lys Ala Thr  
 20 25 30  
 Glu Ala Gly Gly Gly Asn Pro Ser Gly Ile Tyr Ser Ala Ile Ile Ser  
 35 40 45  
 Arg Asn Phe Pro Ile Ile Gly Val Lys Glu Lys Thr Phe Glu Gln Leu  
 50 55 60

His	Lys	Lys	Cys	Leu	Glu	Lys	Lys	Val	Leu	Tyr	Val	Asp	Pro	Glu	Phe	65	70	75	80
Pro	Pro	Asp	Glu	Thr	Ser	Leu	Phe	Tyr	Ser	Gln	Lys	Phe	Pro	Ile	Gln	85	90	95	
Phe	Val	Trp	Lys	Arg	Pro	Pro	Glu	Ile	Cys	Glu	Asn	Pro	Arg	Phe	Ile	100	105	110	
Ile	Asp	Gly	Ala	Asn	Arg	Thr	Asp	Ile	Cys	Gln	Gly	Glu	Leu	Gly	Asp	115	120	125	
Cys	Trp	Phe	Leu	Ala	Ala	Ile	Ala	Cys	Leu	Thr	Leu	Asn	Gln	His	Leu	130	135	140	
Leu	Phe	Arg	Val	Ile	Pro	His	Asp	Gln	Ser	Phe	Ile	Glu	Asn	Tyr	Ala	145	150	155	160
Gly	Ile	Phe	His	Phe	Gln	Phe	Trp	Arg	Tyr	Gly	Glu	Trp	Val	Asp	Val	165	170	175	
Val	Ile	Asp	Asp	Cys	Leu	Pro	Thr	Tyr	Asn	Asn	Gln	Leu	Val	Phe	Thr	180	185	190	
Lys	Ser	Asn	His	Arg	Asn	Glu	Phe	Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala	195	200	205	
Tyr	Ala	Lys	Leu	His	Gly	Ser	Tyr	Glu	Ala	Leu	Lys	Gly	Gly	Asn	Thr	210	215	220	
Thr	Glu	Ala	Met	Glu	Asp	Phe	Thr	Gly	Gly	Val	Ala	Glu	Phe	Phe	Glu	225	230	235	240
Ile	Arg	Asp	Ala	Pro	Ser	Asp	Met	Tyr	Lys	Ile	Met	Lys	Lys	Ala	Ile	245	250	255	
Glu	Arg	Gly	Ser	Leu	Met	Gly	Cys	Ser	Ile	Asp	Asp	Gly	Thr	Asn	Met	260	265	270	
Thr	Tyr	Gly	Thr	Ser	Pro	Ser	Gly	Leu	Asn	Met	Gly	Glu	Leu	Ile	Ala	275	280	285	
Arg	Met	Val	Arg	Asn	Met	Asp	Asn	Ser	Leu	Leu	Gln	Asp	Ser	Asp	Leu	290	295	300	
Asp	Pro	Arg	Gly	Ser	Asp	Glu	Arg	Pro	Thr	Arg	Thr	Ile	Ile	Pro	Val	305	310	315	320
Gln	Tyr	Glu	Thr	Arg	Met	Ala	Cys	Gly	Leu	Val	Arg	Gly	His	Ala	Tyr	325	330	335	
Ser	Val	Thr	Gly	Leu	Asp	Glu	Val	Pro	Phe	Lys	Gly	Glu	Lys	Val	Lys	340	345	350	
Leu	Val	Arg	Leu	Arg	Asn	Pro	Trp	Gly	Gln	Val	Glu	Trp	Asn	Gly	Ser	355	360	365	

Trp	Ser	Asp	Arg	Trp	Lys	Asp	Trp	Ser	Phe	Val	Asp	Lys	Asp	Glu	Lys		
370						375					380						
Ala	Arg	Leu	Gln	His	Gln	Val	Thr	Glu	Asp	Gly	Glu	Phe	Trp	Met	Ser		
385					390					395					400		
Tyr	Glu	Asp	Phe	Ile	Tyr	His	Phe	Thr	Lys	Leu	Glu	Ile	Cys	Asn	Leu		
				405					410					415			
Thr	Ala	Asp	Ala	Leu	Gln	Ser	Asp	Lys	Leu	Gln	Thr	Trp	Thr	Val	Ser		
			420					425						430			
Val	Asn	Glu	Gly	Arg	Trp	Val	Arg	Gly	Cys	Ser	Ala	Gly	Gly	Cys	Arg		
		435					440					445					
Asn	Phe	Pro	Asp	Thr	Phe	Trp	Thr	Asn	Pro	Gln	Tyr	Arg	Leu	Lys	Leu		
	450					455					460						
Leu	Glu	Glu	Asp	Asp	Asp	Pro	Asp	Asp	Ser	Glu	Val	Ile	Cys	Ser	Phe		
465					470					475					480		
Leu	Val	Ala	Leu	Met	Gln	Lys	Asn	Arg	Arg	Lys	Asp	Arg	Lys	Leu	Gly		
				485					490					495			
Ala	Ser	Leu	Phe	Thr	Ile	Gly	Phe	Ala	Ile	Tyr	Glu	Val	Pro	Lys	Glu		
			500					505						510			
Met	His	Gly	Asn	Lys	Gln	His	Leu	Gln	Lys	Asp	Phe	Phe	Leu	Tyr	Asn		
		515					520					525					
Ala	Ser	Lys	Ala	Arg	Ser	Lys	Thr	Tyr	Ile	Asn	Met	Arg	Glu	Val	Ser		
	530					535					540						
Gln	Arg	Phe	Arg	Leu	Pro	Pro	Ser	Glu	Tyr	Val	Ile	Val	Pro	Ser	Thr		
545					550					555					560		
Tyr	Glu	Pro	His	Gln	Glu	Gly	Glu	Phe	Ile	Leu	Arg	Val	Phe	Ser	Glu		
				565					570					575			
Lys	Arg	Asn	Leu	Ser	Glu	Glu	Val	Glu	Asn	Thr	Ile	Ser	Val	Asp	Arg		
			580					585					590				
Pro	Val	Lys	Lys	Lys	Lys	Thr	Lys	Pro	Ile	Ile	Phe	Val	Ser	Asp	Arg		
		595					600					605					
Ala	Asn	Ser	Asn	Lys	Glu	Leu	Gly	Val	Asp	Gln	Glu	Ser	Glu	Glu	Gly		
	610					615					620						
Lys	Gly	Lys	Thr	Ser	Pro	Asp	Lys	Gln	Lys	Gln	Ser	Pro	Gln	Pro	Gln		
625					630					635					640		
Pro	Gly	Ser	Ser	Asp	Gln	Glu	Ser	Glu	Glu	Gln	Gln	Gln	Phe	Arg	Asn		
				645					650					655			
Ile	Phe	Lys	Gln	Ile	Ala	Gly	Asp	Asp	Met	Glu	Ile	Cys	Ala	Asp	Glu		
			660					665						670			

Leu Lys Lys Val Leu Asn Thr Val Val Asn Lys His Lys Asp Leu Lys  
675 680 685

Thr His Gly Phe Thr Leu Glu Ser Cys Arg Ser Met Ile Ala Leu Met  
690 695 700

Asp Thr Asp Gly Ser Gly Lys Leu Asn Leu Gln Glu Phe His His Leu  
705 710 715 720

Trp Asn Lys Ile Lys Ala Trp Gln Lys Ile Phe Lys His Tyr Asp Thr  
725 730 735

Asp Gln Ser Gly Thr Ile Asn Ser Tyr Glu Met Arg Asn Ala Val Asn  
740 745 750

Asp Ala Gly Phe His Leu Asn Asn Gln Leu Tyr Asp Ile Ile Thr Met  
755 760 765

Arg Tyr Ala Asp Lys His Met Asn Ile Asp Phe Asp Ser Phe Ile Cys  
770 775 780

Cys Phe Val Arg Leu Glu Gly Met Phe Arg Ala Phe His Ala Phe Asp  
785 790 795 800

Lys Asp Gly Asp Gly Ile Ile Lys Leu Asn Val Leu Glu Trp Leu Gln  
805 810 815

Leu Thr Met Tyr Ala  
820

<210> 25  
<211> 639  
<212> PRT  
<213> Human

<400> 25

Met Phe Ser Cys Val Lys Pro Tyr Glu Asp Gln Asn Tyr Ser Ala Leu  
1 5 10 15

Arg Arg Asp Cys Arg Arg Arg Lys Val Leu Phe Glu Asp Pro Leu Phe  
20 25 30

Pro Ala Thr Asp Asp Ser Leu Tyr Tyr Lys Gly Thr Pro Gly Pro Ala  
35 40 45

Val Arg Arg Lys Arg Pro Lys Gly Ile Cys Glu Asp Pro Arg Leu Phe  
50 55 60

Val Asp Gly Ile Ser Ser His Asp Leu His Gln Gly Gln Val Gly Asn  
65 70 75 80

Cys Trp Phe Val Ala Ala Cys Ser Ser Leu Ala Ser Arg Glu Ser Leu  
85 90 95

Trp Gln Lys Val Ile Pro Asp Trp Lys Glu Gln Glu Trp Asp Pro Glu

100					105					110					
Lys	Pro	Asn	Ala	Tyr	Ala	Gly	Ile	Phe	His	Phe	His	Phe	Trp	Arg	Phe
		115					120					125			
Gly	Trp	Val	Asp	Val	Val	Ile	Asp	Asp	Arg	Leu	Pro	Thr	Val	Asn	Asn
	130					135					140				
Gln	Leu	Ile	Tyr	Cys	His	Ser	Asn	Ser	Arg	Asn	Glu	Phe	Trp	Cys	Ala
145					150					155					160
Leu	Val	Glu	Lys	Ala	Tyr	Ala	Lys	Leu	Ala	Gly	Cys	Tyr	Gln	Ala	Leu
				165					170					175	
Asp	Gly	Gly	Asn	Thr	Ala	Asp	Ala	Leu	Val	Asp	Phe	Thr	Gly	Gly	Val
			180					185					190		
Ser	Glu	Pro	Ile	Asp	Leu	Thr	Glu	Gly	Asp	Phe	Ala	Asn	Asp	Glu	Thr
		195					200					205			
Lys	Arg	Asn	Gln	Leu	Phe	Glu	Arg	Met	Leu	Lys	Val	His	Ser	Arg	Gly
	210					215					220				
Gly	Leu	Ile	Ser	Ala	Ser	Ile	Lys	Ala	Val	Thr	Ala	Ala	Asp	Met	Glu
225					230					235					240
Ala	Arg	Leu	Ala	Cys	Gly	Leu	Val	Lys	Gly	His	Ala	Tyr	Ala	Val	Thr
				245					250					255	
Asp	Val	Arg	Lys	Val	Arg	Leu	Gly	His	Gly	Leu	Leu	Ala	Phe	Phe	Lys
			260					265					270		
Ser	Glu	Lys	Leu	Asp	Met	Ile	Arg	Leu	Arg	Asn	Pro	Trp	Gly	Glu	Arg
		275					280					285			
Glu	Trp	Asn	Gly	Pro	Trp	Ser	Asp	Thr	Ser	Glu	Glu	Trp	Gln	Lys	Val
	290					295					300				
Ser	Lys	Ser	Glu	Arg	Glu	Lys	Met	Gly	Val	Thr	Val	Gln	Asp	Asp	Gly
305					310					315					320
Glu	Phe	Trp	Met	Thr	Phe	Glu	Asp	Val	Cys	Arg	Tyr	Phe	Thr	Asp	Ile
				325					330					335	
Ile	Lys	Cys	Arg	Val	Ile	Asn	Thr	Ser	His	Leu	Ser	Ile	His	Lys	Thr
			340					345					350		
Trp	Glu	Glu	Ala	Arg	Leu	His	Gly	Ala	Trp	Thr	Leu	His	Glu	Asp	Pro
		355					360					365			
Arg	Gln	Asn	Arg	Gly	Gly	Gly	Cys	Ile	Asn	His	Lys	Asp	Thr	Phe	Phe
	370					375					380				
Gln	Asn	Pro	Gln	Tyr	Ile	Phe	Glu	Val	Lys	Lys	Pro	Glu	Asp	Glu	Val
385					390					395					400
Leu	Ile	Cys	Ile	Gln	Gln	Arg	Pro	Lys	Arg	Ser	Thr	Arg	Arg	Glu	Gly

	405		410		415
Lys Gly Glu Asn Leu Ala Ile Gly Phe Asp Ile Tyr Lys Val Glu Glu					
	420		425		430
Asn Arg Gln Tyr Arg Met His Ser Leu Gln His Lys Ala Ala Ser Ser					
	435		440		445
Ile Tyr Ile Asn Ser Arg Ser Val Phe Leu Arg Thr Asp Gln Pro Glu					
	450		455		460
Gly Arg Tyr Val Ile Ile Pro Thr Thr Phe Glu Pro Gly His Thr Gly					
	465		470		480
Glu Phe Leu Leu Arg Val Phe Thr Asp Val Pro Ser Asn Cys Arg Glu					
	485		490		495
Leu Arg Leu Asp Glu Pro Pro His Thr Cys Trp Ser Ser Leu Cys Gly					
	500		505		510
Tyr Pro Gln Leu Val Thr Gln Val His Val Leu Gly Ala Ala Gly Leu					
	515		520		525
Lys Asp Ser Pro Thr Gly Ala Asn Ser Tyr Val Ile Ile Lys Cys Glu					
	530		535		540
Gly Asp Lys Val Arg Ser Ala Val Gln Lys Gly Thr Ser Thr Pro Glu					
	545		550		560
Tyr Asn Val Lys Gly Ile Phe Tyr Arg Lys Lys Leu Ser Gln Pro Ile					
	565		570		575
Thr Val Gln Val Trp Asn His Arg Val Leu Lys Asp Glu Phe Leu Gly					
	580		585		590
Gln Val His Leu Lys Ala Asp Pro Asp Asn Leu Gln Ala Leu His Thr					
	595		600		605
Leu His Leu Arg Asp Arg Asn Ser Arg Gln Pro Ser Asn Leu Pro Gly					
	610		615		620
Thr Val Ala Val His Ile Leu Ser Ser Thr Ser Leu Met Ala Val					
	625		630		635
<210> 26					
<211> 641					
<212> PRT					
<213> Mus musculus					
<400> 26					
Met Gly Pro Pro Leu Lys Leu Phe Lys Asn Gln Lys Tyr Gln Glu Leu					
1 5 10 15					
Lys Gln Glu Cys Met Lys Asp Gly Arg Leu Phe Cys Asp Pro Thr Phe					
20 25 30					





Leu Asn Val Cys Arg Asn Val Asn Asn Pro Val Phe Gly Arg Lys Glu  
 340 345 350  
 Leu Glu Ser Val Val Gly Cys Trp Thr Val Asp Asp Asp Pro Leu Met  
 355 360 365  
 Asn Arg Ser Gly Gly Cys Tyr Asn Asn Arg Asp Thr Phe Leu Gln Asn  
 370 375 380  
 Pro Gln Tyr Ile Phe Thr Val Pro Glu Asp Gly His Lys Val Ile Met  
 385 390 395 400  
 Ser Leu Gln Gln Lys Asp Leu Arg Thr Tyr Arg Arg Met Gly Arg Pro  
 405 410 415  
 Asp Asn Tyr Ile Ile Gly Phe Glu Leu Phe Lys Val Glu Met Asn Arg  
 420 425 430  
 Arg Phe Arg Leu His His Leu Tyr Ile Gln Glu Arg Ala Gly Thr Ser  
 435 440 445  
 Thr Tyr Ile Asp Thr Arg Thr Val Phe Leu Ser Lys Tyr Leu Lys Lys  
 450 455 460  
 Gly Ser Tyr Val Leu Val Pro Thr Met Phe Gln His Gly Arg Thr Ser  
 465 470 475 480  
 Glu Phe Leu Leu Arg Ile Phe Ser Glu Val Pro Val Gln Leu Arg Glu  
 485 490 495  
 Leu Thr Leu Asp Met Pro Lys Met Ser Cys Trp Asn Leu Ala Arg Gly  
 500 505 510  
 Tyr Pro Lys Val Val Thr Gln Ile Thr Val His Ser Ala Glu Gly Leu  
 515 520 525  
 Glu Lys Lys Tyr Ala Asn Glu Thr Val Asn Pro Tyr Leu Ile Ile Lys  
 530 535 540  
 Cys Gly Lys Glu Glu Val Arg Ser Pro Val Gln Lys Asn Thr Val His  
 545 550 555 560  
 Ala Ile Phe Asp Thr Gln Ala Val Phe Tyr Arg Arg Thr Thr Asp Ile  
 565 570 575  
 Pro Ile Ile Ile Gln Val Trp Asn Ser Arg Lys Phe Cys Asp Gln Phe  
 580 585 590  
 Leu Gly Gln Val Thr Leu Asp Ala Asp Pro Ser Asp Cys Arg Asp Leu  
 595 600 605  
 Lys Ser Leu Tyr Leu Arg Lys Lys Gly Gly Pro Thr Ala Lys Val Lys  
 610 615 620  
 Gln Gly His Ile Ser Phe Lys Val Ile Ser Ser Asp Asp Leu Thr Glu  
 625 630 635 640

Leu

<210> 27  
<211> 703  
<212> PRT  
<213> RAT

<400> 27

Met	Ala	Ala	Leu	Ala	Ala	Gly	Val	Ser	Lys	Gln	Arg	Ala	Val	Ala	Glu	
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Gly	Leu	Gly	Ser	Asn	Gln	Asn	Ala	Val	Lys	Tyr	Leu	Gly	Gln	Asp	Phe	
			20					25					30			
Glu	Thr	Leu	Arg	Lys	Gln	Cys	Leu	Asn	Ser	Gly	Val	Leu	Phe	Lys	Asp	
		35					40					45				
Pro	Glu	Phe	Pro	Ala	Cys	Pro	Ser	Ala	Leu	Gly	Tyr	Lys	Asp	Leu	Gly	
	50					55					60					
Pro	Gly	Ser	Pro	Asp	Thr	Gln	Gly	Ile	Val	Trp	Lys	Arg	Pro	Thr	Glu	
	65				70					75					80	
Leu	Cys	Pro	Asn	Pro	Gln	Phe	Ile	Val	Gly	Gly	Ala	Thr	Arg	Thr	Asp	
				85					90					95		
Ile	Arg	Gln	Gly	Gly	Leu	Gly	Asp	Cys	Trp	Leu	Leu	Ala	Ala	Ile	Ala	
		100						105					110			
Ser	Leu	Thr	Leu	Asn	Glu	Lys	Leu	Leu	Tyr	Arg	Val	Leu	Pro	Arg	Asp	
		115					120					125				
Gln	Ser	Phe	Gln	Lys	Asp	Tyr	Ala	Gly	Ile	Phe	His	Phe	Gln	Phe	Trp	
	130					135					140					
Gln	Tyr	Gly	Glu	Trp	Val	Glu	Val	Val	Ile	Asp	Asp	Arg	Leu	Pro	Thr	
	145				150					155					160	
Lys	Asn	Gly	Gln	Leu	Leu	Phe	Leu	His	Ser	Glu	Glu	Gly	Asn	Glu	Phe	
			165						170					175		
Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala	Tyr	Ala	Lys	Leu	Asn	Gly	Ser	Tyr	
		180						185					190			
Glu	Ala	Leu	Val	Gly	Gly	Ser	Thr	Ile	Glu	Gly	Phe	Glu	Asp	Phe	Thr	
		195					200					205				
Gly	Gly	Ile	Ser	Glu	Phe	Tyr	Asp	Leu	Lys	Lys	Pro	Pro	Glu	Asn	Leu	
	210					215					220					
Tyr	Tyr	Ile	Ile	Gln	Lys	Ala	Leu	Arg	Lys	Gly	Ser	Leu	Leu	Gly	Cys	
	225				230					235					240	
Ser	Ile	Asp	Val	Ser	Thr	Ala	Ala	Glu	Ala	Glu	Ala	Thr	Thr	Arg	Gln	
			245					250						255		

Lys	Leu	Val	Lys	Gly	His	Ala	Tyr	Ser	Val	Thr	Gly	Val	Glu	Glu	Val			
			260					265					270					
Asn	Phe	His	Gly	Arg	Pro	Glu	Lys	Leu	Ile	Arg	Leu	Arg	Asn	Pro	Trp			
		275					280					285						
Gly	Glu	Val	Glu	Trp	Ser	Gly	Ala	Trp	Ser	Asp	Asn	Ala	Pro	Glu	Trp			
	290					295					300							
Asn	Tyr	Ile	Asp	Pro	Arg	Arg	Lys	Glu	Glu	Leu	Asp	Lys	Lys	Ala	Glu			
305					310					315					320			
Asp	Gly	Glu	Phe	Trp	Met	Ser	Phe	Ser	Asp	Phe	Leu	Lys	Gln	Tyr	Ser			
			325						330					335				
Arg	Leu	Glu	Ile	Cys	Asn	Leu	Ser	Pro	Asp	Ser	Leu	Ser	Ser	Glu	Glu			
			340					345					350					
Ile	His	Lys	Trp	Asn	Leu	Val	Leu	Phe	Asn	Gly	Arg	Trp	Thr	Arg	Gly			
		355					360					365						
Ser	Thr	Ala	Gly	Gly	Cys	Leu	Asn	Tyr	Pro	Gly	Thr	Tyr	Trp	Thr	Asn			
	370					375					380							
Pro	Gln	Phe	Lys	Ile	His	Leu	Asp	Glu	Val	Asp	Glu	Asp	Gln	Glu	Glu			
385					390					395					400			
Gly	Thr	Ser	Glu	Pro	Cys	Cys	Thr	Val	Leu	Leu	Gly	Leu	Met	Gln	Lys			
				405					410					415				
Asn	Arg	Arg	Arg	Gln	Lys	Arg	Ile	Gly	Gln	Gly	Met	Leu	Ser	Ile	Gly			
			420					425					430					
Tyr	Ala	Val	Tyr	Gln	Ile	Pro	Lys	Glu	Leu	Glu	Ser	His	Thr	Asp	Ala			
		435					440					445						
His	Leu	Gly	Arg	Asp	Phe	Phe	Leu	Gly	Arg	Gln	Pro	Ser	Thr	Cys	Ser			
	450					455					460							
Ser	Thr	Tyr	Met	Asn	Leu	Arg	Glu	Val	Ser	Ser	Arg	Val	Arg	Leu	Pro			
465					470					475					480			
Pro	Gly	Gln	Tyr	Leu	Val	Val	Pro	Ser	Thr	Phe	Glu	Pro	Phe	Lys	Asp			
				485					490					495				
Gly	Asp	Phe	Cys	Leu	Arg	Val	Phe	Ser	Glu	Lys	Lys	Ala	Lys	Ala	Leu			
			500					505					510					
Glu	Ile	Gly	Asp	Thr	Val	Ser	Gly	His	Pro	His	Glu	Pro	His	Pro	Arg			
		515					520					525						
Asp	Met	Asp	Glu	Glu	Asp	Glu	His	Val	Arg	Ser	Leu	Phe	Glu	Glu	Phe			
	530					535					540							
Val	Gly	Lys	Asp	Ser	Glu	Ile	Ser	Ala	Asn	Gln	Leu	Lys	Arg	Val	Leu			
545					550					555					560			

Asn Glu Val Leu Ser Lys Arg Thr Asp Met Lys Phe Asp Gly Phe Asn  
565 570 575

Ile Asn Thr Cys Arg Glu Met Ile Ser Leu Leu Asp Ser Asp Gly Thr  
580 585 590

Gly Ser Leu Gly Pro Met Glu Phe Lys Thr Leu Trp Leu Lys Ile Arg  
595 600 605

Thr Tyr Leu Glu Ile Phe Gln Glu Met Asp His Asn His Val Gly Thr  
610 615 620

Ile Glu Ala His Glu Met Arg Thr Ala Leu Lys Lys Ala Gly Phe Thr  
625 630 635 640

Leu Asn Asn Gln Val Gln Gln Thr Ile Ala Met Arg Tyr Ala Cys Ser  
645 650 655

Lys Leu Gly Val Asp Phe Asn Gly Phe Val Ala Cys Met Ile Arg Leu  
660 665 670

Glu Thr Leu Phe Lys Leu Phe Arg Leu Leu Asp Lys Asp Gln Asn Gly  
675 680 685

Ile Val Gln Leu Ser Leu Ala Glu Trp Leu Cys Cys Val Leu Val  
690 695 700

<210> 28

<211> 690

<212> PRT

<213> Human

<400> 28

Met Pro Tyr Leu Tyr Arg Ala Pro Gly Pro Gln Ala His Pro Val Pro  
1 5 10 15

Lys Asp Ala Arg Ile Thr His Ser Ser Gly Gln Ser Phe Glu Gln Met  
20 25 30

Arg Gln Glu Cys Leu Gln Arg Gly Thr Leu Phe Glu Asp Ala Asp Phe  
35 40 45

Pro Ala Ser Asn Ser Ser Leu Phe Tyr Ser Glu Arg Pro Gln Ile Pro  
50 55 60

Phe Val Trp Lys Arg Pro Gly Glu Ile Val Lys Asn Pro Glu Phe Ile  
65 70 75 80

Leu Gly Gly Ala Thr Arg Thr Asp Ile Cys Gln Gly Glu Leu Gly Asp  
85 90 95

Cys Trp Leu Leu Ala Ala Ile Ala Ser Leu Thr Leu Asn Gln Lys Ala  
100 105 110

Leu Ala Arg Val Ile Pro Gln Asp Gln Ser Phe Gly Pro Gly Tyr Ala

115					120					125					
Gly	Ile	Phe	His	Phe	Gln	Phe	Trp	Gln	His	Ser	Glu	Trp	Leu	Asp	Val
130						135					140				
Val	Ile	Asp	Asp	Arg	Leu	Pro	Thr	Phe	Arg	Asp	Arg	Leu	Val	Phe	Leu
145					150					155					160
His	Ser	Ala	Asp	His	Asn	Glu	Phe	Trp	Ser	Ala	Leu	Leu	Glu	Lys	Ala
				165					170					175	
Tyr	Ala	Lys	Leu	Asn	Gly	Ser	Tyr	Glu	Ala	Leu	Lys	Gly	Gly	Ser	Ala
			180					185					190		
Ile	Glu	Ala	Met	Glu	Asp	Phe	Thr	Gly	Gly	Val	Ala	Glu	Thr	Phe	Gln
		195					200					205			
Thr	Lys	Glu	Ala	Pro	Glu	Asn	Phe	Tyr	Glu	Ile	Leu	Glu	Lys	Ala	Leu
	210					215					220				
Lys	Arg	Gly	Ser	Leu	Leu	Gly	Cys	Phe	Ile	Asp	Thr	Arg	Ser	Ala	Ala
225					230					235					240
Glu	Ser	Glu	Ala	Arg	Thr	Pro	Phe	Gly	Leu	Ile	Lys	Gly	His	Ala	Tyr
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Ser	Val	Thr	Gly	Ile	Asp	Gln	Val	Ser	Phe	Arg	Gly	Gln	Arg	Ile	Glu
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Leu	Ile	Arg	Ile	Arg	Asn	Pro	Trp	Gly	Gln	Val	Glu	Trp	Asn	Gly	Ser
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Trp	Ser	Asp	Ser	Ser	Pro	Glu	Trp	Arg	Ser	Val	Gly	Pro	Ala	Glu	Gln
		290				295					300				
Lys	Arg	Leu	Cys	His	Thr	Ala	Leu	Asp	Asp	Gly	Glu	Phe	Trp	Met	Ala
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Phe	Lys	Asp	Phe	Lys	Ala	His	Phe	Asp	Lys	Val	Glu	Ile	Cys	Asn	Leu
				325					330					335	
Thr	Pro	Asp	Ala	Leu	Glu	Glu	Asp	Ala	Ile	His	Lys	Trp	Glu	Val	Thr
			340					345					350		
Val	His	Gln	Gly	Ser	Trp	Val	Arg	Gly	Ser	Thr	Ala	Gly	Gly	Cys	Arg
		355					360					365			
Asn	Phe	Leu	Asp	Thr	Phe	Trp	Thr	Asn	Pro	Gln	Ile	Lys	Leu	Ser	Leu
	370					375					380				
Thr	Glu	Lys	Asp	Glu	Gly	Gln	Glu	Glu	Cys	Ser	Phe	Leu	Val	Ala	Leu
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Met	Gln	Lys	Asp	Arg	Arg	Lys	Leu	Lys	Arg	Phe	Gly	Ala	Asn	Val	Leu
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Thr	Ile	Gly	Tyr	Ala	Ile	Tyr	Glu	Cys	Pro	Asp	Lys	Asp	Glu	His	Leu

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Asn	Lys	Asp	Phe	Phe	Arg	Tyr	His	Ala	Ser	Arg	Ala	Arg	Ser	Lys	Thr
		435					440					445			
Phe	Ile	Asn	Leu	Arg	Glu	Val	Ser	Asp	Arg	Phe	Lys	Leu	Pro	Pro	Gly
	450					455					460				
Glu	Tyr	Ile	Leu	Ile	Pro	Ser	Thr	Phe	Glu	Pro	His	Gln	Glu	Ala	Asp
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Phe	Cys	Leu	Arg	Ile	Phe	Ser	Glu	Lys	Lys	Ala	Ile	Thr	Arg	Asp	Met
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Asp	Gly	Asn	Val	Asp	Ile	Asp	Leu	Pro	Glu	Pro	Pro	Lys	Pro	Thr	Pro
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Pro	Asp	Gln	Glu	Thr	Glu	Glu	Glu	Gln	Arg	Phe	Arg	Ala	Leu	Phe	Glu
	515						520					525			
Gln	Val	Ala	Gly	Glu	Asp	Met	Glu	Val	Thr	Ala	Glu	Glu	Leu	Glu	Tyr
	530					535					540				
Val	Leu	Asn	Ala	Val	Leu	Gln	Lys	Lys	Lys	Asp	Ile	Lys	Phe	Lys	Lys
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Leu	Ser	Leu	Ile	Ser	Cys	Lys	Asn	Ile	Ile	Ser	Leu	Met	Asp	Thr	Ser
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Gly	Asn	Gly	Lys	Leu	Glu	Phe	Asp	Glu	Phe	Lys	Val	Phe	Trp	Asp	Lys
			580					585					590		
Leu	Lys	Gln	Trp	Ile	Asn	Leu	Phe	Leu	Arg	Phe	Asp	Ala	Asp	Lys	Ser
		595					600					605			
Gly	Thr	Met	Ser	Thr	Tyr	Glu	Leu	Arg	Thr	Ala	Leu	Lys	Ala	Ala	Gly
	610					615					620				
Phe	Gln	Leu	Ser	Ser	His	Leu	Leu	Gln	Leu	Ile	Val	Leu	Arg	Tyr	Ala
625					630					635					640
Asp	Glu	Glu	Leu	Gln	Leu	Asp	Phe	Asp	Asp	Phe	Leu	Asn	Cys	Leu	Val
				645					650					655	
Arg	Leu	Glu	Asn	Ala	Ser	Arg	Val	Phe	Gln	Ala	Leu	Ser	Thr	Lys	Asn
			660					665					670		
Lys	Glu	Phe	Ile	His	Leu	Asn	Ile	Asn	Glu	Phe	Ile	His	Leu	Thr	Met
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